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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,161	09/10/2001	Tsunetoshi Honma	067242-0152	9225

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 02/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,161	HONMA ET AL.	
	Examiner	Art Unit	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,11-15 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,11-15 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 8, 11-15 and 19 are pending in the application.

This action is in response to applicant's amendment filed November 17, 2003. Claims 8, 11-15 and 19 were amended and claims 9, 10 and 16-18 were canceled.

Response to Amendment

Applicant's arguments filed November 17, 2003 have been fully considered with the following effect:

1. The applicants amendments are sufficient to overcome the 35 USC § 112, first paragraph rejection labeled paragraph 3 of the last office action, which is hereby **withdrawn**.

2. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled 4a) and 4b) of the last office action, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejection labeled c) the applicant's amendments and remarks have been fully considered but they are not persuasive.

c) The applicant's stated that the phrase "an effective amount of" has been added to claim 19. However, claim 19 still fails to recite whether this is indicative of a subject in need thereof.

Claim 19 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For reasons of record and stated above.

3. The applicant's amendments are sufficient to overcome the 35 USC § 101 rejection labeled paragraph 5 of the last office action, which is hereby **withdrawn**.

4. The applicant's amendments are sufficient to overcome the 35 USC § 102, anticipation rejection labeled paragraph 6 of the last office action, which is hereby **withdrawn**.

5. The applicant's amendments are sufficient to overcome the 35 USC § 103, obviousness rejection labeled paragraph 7 of the last office action, which is hereby **withdrawn**.

6. With regards to the obviousness-type double patenting rejection as being unpatentable over U.S. Patent No. 6,384,075 and U.S. Patent No. 6,172,113 of the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive. The applicant's stated that the compounds of amended claim 8 is unobvious over U.S. Patent No. 6,384,075 and U.S. Patent No. 6,172,113 because the compound has an antagonistic activity against not only a PGD2 receptor but also a TXA2 receptor. The use of the compounds in the reference is irrelevant with respect to the compound claims of the instant invention. It's the compounds which are being claimed in claims 8 and 11-13 versus the compound claims of U.S. '075. Additionally, just as the discovery of a new property does not make an old compound patentable, so does the discovery a new mechanism of action make an old use patentable. Ex parte Novitski 26 USPQ2d 1389. A process claim is anticipated even if patentee of prior art did not recognize that an "inventive concept" of the new claim was present in the prior

art, Verdegaal Brothers Inc. v. Union Oil Company of California 2 USPQ2d 1051. Mehl/Biophile International Corp. v. Milgraum 52 USPQ2d 1303, "[i]nherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art."

Claims 8, 11-15 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 7-11 of U.S. Patent No. 6,384,075. For reasons of record and stated above.

Claims 15 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5 and 6 of U.S. Patent No. 6,172,113. For reasons of record and stated above.

7. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/297,065 of the last office action, the applicant's remarks have been fully considered but they are not persuasive. The applicant's stated that when the only rejection remaining is a provisional double patenting rejection, the Examiner should withdraw the rejection and allow the application to issue as a patent. However, this is not the only issue remaining.

Claims 8, 11-15 and 19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3 and 8-22 of copending Application No. 10/297,065. For reasons of record and stated above.

In view of the amendment dated November 17, 2003, the following new grounds of rejection apply:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 15 is vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by inhibiting the activity of PGD_2 and/or TXA_2 receptors. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties in vitro, when administered to a patient with a certain disease, does not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in

100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus iv or in a time release po formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active in vitro, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of which are inhibitors in vitro, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the

accurate answer, and that the success of second compound arises from some other unknown property, which the second drug is capable. It is common for a drug, particularly in anti-thrombotics and mast cell dysfunction, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to affect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy, which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 8, 11-15 and 19 are rejected under 35 U.S.C. 103(a) as being obvious over WO 97/00853 (U.S. equivalents 6,384,075 and 6,172,113). The generic structure of WO 97/00853 encompasses the instantly claimed compounds (see Formula I, column 2) and for the same uses as claimed herein. Examples in Table 2a differ only in the nature of the Y=, m, Z, A, B, R, X1, X2 and X3 substituents. Column 2, lines 20-62 defines the substituent Y= as a bicyclic ring, i.e.[2.2.1]cycloheptane, dimethyl substituted [3.1.1]cycloheptane, etc., A is alkylene which is intervened by hetero atom or phenylene, contains oxo group, and/or has an unsaturated bond; B is hydrogen, alkyl, aralkyl or acyl; R is COOR1, CH2OR2 or CON(R3)R4; X1 is a single bond, phenylene, naphtylene, thiophenediyl, indolediyl, or oxazolediyl; X2 is a single bond, -N=N-, -N=CH-, -CH=N-, etc., and X3 is alkyl, alkenyl, alkynyl, aryl, aralkyl, heterocyclic group, cycloalkyl, etc. Compounds of the instant invention are generically embraced by Ohtani in view of the interchange ability of Y=, A, R, X1, X2 and X3 substituents of the bicyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example Y= is ring [2.2.1]cycloheptane, m is 0, X2 is -N=N-, R2 is H or Me as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:00-5:30 Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 571-272-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting -SPE of 1624 at 571-272-0661.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brenda Coleman

Brenda Coleman
Primary Examiner Art Unit 1624
January 30, 2004